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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/528,451	03/18/2005	Akihiro Uchida	00005.001257.	4278

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EXAMINER	
SASAN, ARADHANA	
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1615	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/528,451	UCHIDA ET AL.	
	Examiner	Art Unit	
	ARADHANA SASAN	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 October 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 6-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 6-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. The remarks and amendments filed on 10/30/08 are acknowledged.

2. Claims 1 and 6-12 are included in the prosecution.

Information Disclosure Statement

3. The information in the supplemental disclosure statement filed on 07/14/05 was noted. However, the information was not listed in Form PTO-1449.

Response to Arguments

Claim Objections

4. In light of Applicant's amendment, the objection to claim 12 is withdrawn.

Rejection of claims 7-12 under 35 USC § 112, second paragraph

5. In light of Applicant's amendments, the rejection of claims 7-12 under 35 USC § 112 are withdrawn.

Rejection of claims 1, 6-8, 10 and 12 under 35 USC § 103(a)

6. Applicant's arguments, see Pages 7-11, filed 10/30/08, with respect to:

- the rejection of claims 1, 6-8, 10 and 12 under 35 USC § 103(a) as being unpatentable over Shimada et al. (Bioorganic & Medicinal Chemistry Letters, Vol. 7, No. 18, pp. 2349-2352, 1997) in view of Sako et al. (US 6,562,375)
- the rejection of claims 9-11 under 35 U.S.C. 103(a) as being unpatentable over Shimada et al. (Bioorganic & Medicinal Chemistry Letters, Vol. 7, No. 18, pp. 2349-2352, 1997) in view of Sako et al. (US 6,562,375) and Okuda et al. (US 4,654,206)

- the rejection of claims 1, 6-8, 10 and 12 under 35 U.S.C. 103(a) as being unpatentable over Suzuki et al. (US 5,484,920) in view of Shimada et al. (Bioorganic & Medicinal Chemistry Letters, Vol. 7, No. 18, pp. 2349-2352, 1997) and Sako et al. (US 6,562,375)
- the rejection of claims 9-11 under 35 U.S.C. 103(a) as being unpatentable over Suzuki et al. (US 5,484,920) in view of Shimada et al. (Bioorganic & Medicinal Chemistry Letters, Vol. 7, No. 18, pp. 2349-2352, 1997), Sako et al. (US 6,562,375) and Okuda et al. (US 4,654,206)
- the rejection of claims 1, 6-8, 10 and 12 under 35 U.S.C. 103(a) as being unpatentable over Hara et al. (WO 01/32182) in view of Shimada et al. (Bioorganic & Medicinal Chemistry Letters, Vol. 7, No. 18, pp. 2349-2352, 1997) and Sako et al. (US 6,562,375)
- the rejection of claims 9-11 under 35 U.S.C. 103(a) as being unpatentable over Hara et al. (WO 01/32182) in view of Shimada et al. (Bioorganic & Medicinal Chemistry Letters, Vol. 7, No. 18, pp. 2349-2352, 1997), Sako et al. (US 6,562,375) and Okuda et al. (US 4,654,206)

have been fully considered and are persuasive. Therefore, the rejections have been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of Harrison et al. (US 5,573,776).

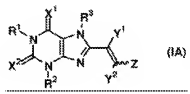
Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 1, 6-8, 10 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shimada et al. (Bioorganic & Medicinal Chemistry Letters, Vol. 7, No. 18, pp. 2349-2352, 1997) in view of Sako et al. (US 6,562,375) and Harrison et al. (US 5,573,776).

The claimed invention is a method for suppressing dimerization of a xanthine compound represented by formula (IA)



(IA)

(wherein Y^1 and Y^2 may be the same or different, and each represents a hydrogen atom, halogen or lower alkyl; Z represents substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl; R^1, R^2 and R^3 may be the same or different and each represents a hydrogen atom, lower alkyl, lower alkenyl or lower alkynyl; and X^1 and X^2 may be the same or different and each represents an oxygen atom or a sulfur atom) or a pharmaceutically acceptable salt thereof, in a solid formulation containing the xanthine compound or the pharmaceutically acceptable salt thereof, which comprises providing iron oxide in the solid formulation, wherein dimerization of the xanthine compound or the pharmaceutically acceptable salt is suppressed.

Shimada teaches 8-styrylxanthines which are adenosine A_{2A} antagonists (Abstract). Shimada teaches that (E)-8-styrylxanthines undergo rapid isomerization

when exposed to light in a dilute solution (Page 2350). (E)-1,3-dialkyl-8-styryl-7-methylxanthine is disclosed (Page 2350). Table 1, compound 6 discloses the elected species - (E)-8-(3,4-dimethoxystyryl)-1,3-diethyl-7-methyl-3,7-dihydro-1H-purine-2,6-dione (Page 2351).

Shimada does not expressly teach a method for suppressing dimerization by providing iron oxide in a solid formulation containing a xanthine compound of formula (IA).

Sako teaches "a method of producing a stable preparation with which there are no changes in drug release in matrix type sustained-release preparations containing polyethylene oxide" (Col. 2, lines 3-6). Sako teaches that "changes in drug release from a preparation can be prevented by adding yellow ferric oxide or red ferric oxide not only by means of physical mixing, but also by means of coating a tablet" (Col. 2, lines 21-25). "There are no special restrictions to the drug used in the present invention as long as it is a drug used in sustained-release preparations that contain polyethylene oxide as one of its base components" (Col. 3, lines 44-47). "Other additives that are pharmaceutically acceptable can be added as needed to the pharmaceutical composition" (Col. 6, lines 58-59). Talc, zinc oxide and magnesium oxide are disclosed as pharmaceutically acceptable additives that can be added to the composition (Col. 6, line 67 and Col. 7, lines 10-11).

Harrison teaches a controlled delivery device comprising an active drug that allows it to be retained in the oral cavity for an extended period of time (Col. 5, lines 16-53). The active drugs include xanthine derivatives (Col. 11, lines 8-31). The controlled

release delivery device also includes polyethylene oxide as a gelling or suspending agent (Col. 12, lines 55-66 and Examples 1, 2, 4 and 8).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make the xanthine compound ((E)-8-(3,4-dimethoxystyryl)-1,3-diethyl-7-methylxanthine), as suggested by Shimada, combine it with the method of stabilization of sustained release pharmaceutical preparations containing drugs and polyethylene oxide by incorporating iron oxide, as taught by Sako, based on the controlled release composition comprising xanthine derivatives and polyethylene oxide, as taught by Harrison, and produce the instant invention.

One of ordinary skill in the art would do this because there is no restriction on the drug used in the sustained release pharmaceutical preparation of Sako. One of ordinary skill in the art would apply the method of stabilizing a sustained or controlled release pharmaceutical preparation with any active or drug. Since a controlled release pharmaceutical preparation comprising xanthine derivatives and polyethylene oxide was known in the art (as evidenced by Harrison), one of ordinary skill in the art would find it obvious to apply the method of stabilizing a controlled release pharmaceutical preparation for enhanced stability. Although Harrison does not expressly teach the elected species, it discloses the genus of xanthine derivatives in a controlled release preparation. One of ordinary skill in the art would find it obvious to incorporate the elected species, as disclosed by Shimada, in a controlled release preparation with polyethylene oxide, because Harrison teaches that xanthine derivatives can be combined with polyethylene oxide.

Moreover, instant claims require suppression of dimerization. However, the cause of such dimerization is not specified in the claims. The instant Specification discloses that impurities can be due to isomerization or dimerization (Page 2, 2nd full paragraph) and that stability of the diarylvinylene compounds is increased by stabilization (Page 3, 1st full paragraph). The end result is improving stability.

Although Sako does not recognize the process or the cause by which stability is improved, Sako achieves the same end result as that of the application, i.e. improving stability. One of ordinary skill in the art would therefore be motivated to use the method of Sako in improving stability of a pharmaceutical preparation.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Regarding instant claim 1, the xanthine compound represented by formula (IA) would have been obvious over the xanthine compound ((E)-1,3-dialkyl-8-styryl-7-methylxanthine) taught by Shimada (Page 2350). The method of suppressing dimerization would have been obvious over the stabilization of controlled release pharmaceutical compositions comprising any active or drug by adding iron oxide, as taught by Sako (Col. 2, lines 2-10 and 21-25) and over the controlled release device comprising drugs such as xanthine derivatives and polyethylene oxide as a suspending

agent as taught by Harrison (Col. 5, lines 16-53, Col. 11, lines 8-31 and Col. 12, lines 55-66 and Examples 1, 2, 4 and 8).

Regarding instant claims 6-7, the elected species of the xanthine compound (E)-8-(3,4-dimethoxystyryl)-1,3-diethyl-7-methyl-3,7-dihydro-1H-purine-2,6-dione would have been obvious over compound no. 6 taught by Shimada (Page 2351, Table 1).

Regarding instant claim 8, the limitation of the solid formulation with a core containing the xanthine compound and a coated layer containing the iron oxide would have been obvious over the xanthine compound taught by Shimada (Page 2351, Table 1), in view of the yellow ferric oxide or red ferric oxide coated on a tablet, as taught by Sako (Col. 2, lines 21-25) and over the compartment of the delivery device that contains the drug, as taught by Harrison (Col. 5, lines 23-27).

Regarding instant claims 10 and 12, the limitations of the percent by weight of iron oxide by weight of the coated layer would have been obvious over the 0.3 to 2 wt% of yellow ferric oxide and/or red ferric oxide in the film coating of the tablet taught by Sako (Col. 10, lines 52-53).

9. Claims 9 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shimada et al. (Bioorganic & Medicinal Chemistry Letters, Vol. 7, No. 18, pp. 2349-2352, 1997) in view of Sako et al. (US 6,562,375), Harrison et al. (US 5,573,776) and Okuda et al. (US 4,654,206).

The teachings of Shimada, Sako and Harrison are stated above.

Shimada, Sako and Harrison do not expressly teach the inclusion of inorganic substances in the coating layer.

Okuda teaches a coating layer on a solid preparation that contains yellow iron oxide and inorganic substances including talc and titanium oxide (Col. 4, lines 36-40).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make the xanthine compound ((E)-8-(3,4-dimethoxystyryl)-1,3-diethyl-7-methylxanthine), as suggested by Shimada, combine it with the method of stabilization of sustained release pharmaceutical preparations containing drugs and polyethylene oxide by incorporating iron oxide, as taught by Sako, based on the controlled release composition comprising xanthine derivatives and polyethylene oxide, as taught by Harrison, further combine it with the use of iron oxide and inorganic substances in the coating layer of a solid pharmaceutical preparation, as taught by Okuda, and produce the instant invention.

One of ordinary skill in the art would do this because it would be obvious to try to include inorganic substances (disclosed by Sako) in the coating layer (taught by Okuda), and have a reasonable expectation of stabilizing a controlled release preparation containing the xanthine compound ((E)-8-(3,4-dimethoxystyryl)-1,3-diethyl-7-methylxanthine).

Regarding instant claim 9, the limitation of an inorganic substance in the coated layer would have been obvious over the additives that can be added to the iron oxide coated pharmaceutical compositions including talc, zinc oxide and magnesium oxide, as taught by Sako (Col. 6, line 58 to Col. 7, line 11) in view of the incorporation of talc and

titanium oxide in the coating layer of solid preparations, as taught by Okuda (Col. 4, lines 36-40).

Regarding instant claim 11, the limitation of the coated layer containing 0.01 to 90 parts by weight inorganic substance per 100 parts by weight of the coated layer would have been obvious to one of ordinary skill in the art because during the process of routine experimentation, one would add different levels of the inorganic substances (such as talc, zinc oxide and magnesium oxide) that are taught by Sako (Col. 6, line 67 and Col. 7, lines 10-11) in view of the incorporation of talc and titanium oxide in the coating layer of solid preparations, as taught by Okuda (Col. 4, lines 36-40).

10. Claims 1, 6-8, 10 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Suzuki et al. (US 5,484,920) in view of Sako et al. (US 6,562,375) and Harrison et al. (US 5,573,776).

Suzuki teaches (E)-8-(3,4-Dimethoxystyryl)-1,3-diethyl-7-methylxanthine (Col. 55, Example 8 and Col. 19, Compound 65).

Suzuki does not expressly teach a method for suppressing dimerization by providing iron oxide in a solid formulation containing a xanthine compound of formula (IA).

The teaching of Sako with respect to the method of stabilization of controlled release pharmaceutical preparations by incorporating iron oxide (Col. 2, lines 3-6 and lines 21-25) is stated above.

The teaching of Harrison with respect to controlled release compositions comprising xanthine derivatives and polyethylene oxide is stated above.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make the xanthine compound ((E)-8-(3,4-dimethoxystyryl)-1,3-diethyl-7-methylxanthine), as suggested by Suzuki, combine it with the method of stabilization of sustained release pharmaceutical preparations containing drugs and polyethylene oxide by incorporating iron oxide, as taught by Sako, based on the controlled release composition comprising xanthine derivatives and polyethylene oxide, as taught by Harrison, and produce the instant invention.

One of ordinary skill in the art would do this because there is no restriction on the drug used in the sustained release pharmaceutical preparation of Sako. One of ordinary skill in the art would apply the method of stabilizing a sustained or controlled release pharmaceutical preparation with any active or drug. Since a controlled release pharmaceutical preparation comprising xanthine derivatives and polyethylene oxide was known in the art (as evidenced by Harrison), one of ordinary skill in the art would find it obvious to apply the method of stabilizing a controlled release pharmaceutical preparation for enhanced stability. Although Harrison does not expressly teach the elected species, it discloses the genus of xanthine derivatives in a controlled release preparation. One of ordinary skill in the art would find it obvious to incorporate the elected species, as disclosed by Suzuki, in a controlled release preparation with polyethylene oxide, because Harrison teaches that xanthine derivatives can be combined with polyethylene oxide.

Regarding instant claim 1, the xanthine compound represented by formula (IA) would have been obvious over the xanthine compound (E)-8-(3,4-Dimethoxystyryl)-1,3-diethyl-7-methylxanthine taught by Suzuki (Col. 55, Example 8 and Col. 19, Compound 65). The method of suppressing dimerization would have been obvious over the stabilization of pharmaceutical compositions by adding iron oxide, as taught by Sako (Col. 2, lines 21-25) and over the controlled release device comprising drugs such as xanthine derivatives and polyethylene oxide as a suspending agent as taught by Harrison (Col. 5, lines 16-53, Col. 11, lines 8-31 and Col. 12, lines 55-66 and Examples 1, 2, 4 and 8).

Regarding instant claims 6-7, the elected species of the xanthine compound (E)-8-(3,4-dimethoxystyryl)-1,3-diethyl-7-methyl-3,7-dihydro-1H-purine-2,6-dione would have been obvious over the ((E)-8-(3,4-dimethoxystyryl)-1,3-diethyl-7-methylxanthine) taught by Suzuki (Col. 55, Example 8 and Col. 19, Compound 65).

Regarding instant claim 8, the limitation of the solid formulation with a core containing the xanthine compound and a coated layer containing the iron oxide would have been obvious over the xanthine compound taught by Suzuki (Col. 55, Example 8 and Col. 19, Compound 65), in view of the yellow ferric oxide or red ferric oxide coated on a tablet, as taught by Sako (Col. 2, lines 21-25).

Regarding instant claims 10 and 12, the limitations of the percent by weight of iron oxide by weight of the coated layer would have been obvious over the 0.3 to 2 wt% of yellow ferric oxide and/or red ferric oxide in the film coating of the tablet taught by Sako (Col. 10, lines 52-53).

11. Claims 9 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Suzuki et al. (US 5,484,920) in view of Sako et al. (US 6,562,375), Harrison et al. (US 5,573,776) and Okuda et al. (US 4,654,206).

The teachings of Suzuki, Sako and Harrison are stated above.

Suzuki, Sako and Harrison do not expressly teach the inclusion of inorganic substances in the coating layer.

Okuda teaches a coating layer on a solid preparation that contains yellow iron oxide and inorganic substances including talc and titanium oxide (Col. 4, lines 36-40).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to (E)-8-(3,4-dimethoxystyryl)-1,3-diethyl-7-methylxanthine), as taught by Suzuki, combine it with the method of stabilization of sustained release pharmaceutical preparations containing drugs and polyethylene oxide by incorporating iron oxide, as taught by Sako, based on the controlled release composition comprising xanthine derivatives and polyethylene oxide, as taught by Harrison, further combine it with the use of iron oxide and inorganic substances in the coating layer of a solid pharmaceutical preparation, as taught by Okuda, and produce the instant invention.

One of ordinary skill in the art would do this because it would be obvious to try to include inorganic substances (disclosed by Sako) in the coating layer (taught by Okuda), and have a reasonable expectation of stabilizing the preparation containing the xanthine compound ((E)-8-(3,4-dimethoxystyryl)-1,3-diethyl-7-methylxanthine).

Regarding instant claim 9, the limitation of an inorganic substance in the coated layer would have been obvious over the additives that can be added to the iron oxide

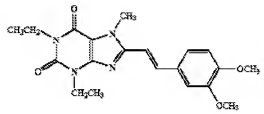
coated pharmaceutical compositions including talc, zinc oxide and magnesium oxide, as taught by Sako (Col. 6, line 58 to Col. 7, line 11) in view of the incorporation of talc and titanium oxide in the coating layer of solid preparations, as taught by Okuda (Col. 4, lines 36-40).

Regarding instant claim 11, the limitation of the coated layer containing 0.01 to 90 parts by weight inorganic substance per 100 parts by weight of the coated layer would have been obvious to one of ordinary skill in the art because during the process of routine experimentation, one would add different levels of the inorganic substances (such as talc, zinc oxide and magnesium oxide) that are taught by Sako (Col. 6, line 67 and Col. 7, lines 10-11) in view of the incorporation of talc and titanium oxide in the coating layer of solid preparations, as taught by Okuda (Col. 4, lines 36-40).

12. Claims 1, 6-8, 10 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hara et al. (WO 01/32182) in view of Sako et al. (US 6,562,375) and Harrison et al. (US 5,573,776).

Regarding the Hara reference, the corresponding US patent application publication (US 2005/0176739 A1 is being used as a reference since an English translation of the WIPO document (WO 01/32182) was not available.

Hara teaches a xanthine derivative as an active ingredient for eating disorders (Abstract). The compound (E)-8-(3,4-dimethoxystyryl)-1,3-diethyl-7-methylxanthine is disclosed (Page 3, [0027]). The structure of this compound is disclosed (Page 2, Table 1, Compound No. 1):



Hara does not expressly teach a method for suppressing dimerization by providing iron oxide in a solid formulation containing a xanthine compound of formula (IA).

The teaching of Sako with respect to the method of stabilization of controlled release pharmaceutical preparations by incorporating iron oxide (Col. 2, lines 3-6 and lines 21-25) is stated above.

The teaching of Harrison with respect to controlled release compositions comprising xanthine derivatives and polyethylene oxide is stated above.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make the xanthine compound ((E)-8-(3,4-dimethoxystyryl)-1,3-diethyl-7-methylxanthine), as suggested by Hara, combine it with the method of stabilization of sustained release pharmaceutical preparations containing drugs and polyethylene oxide by incorporating iron oxide, as taught by Sako, based on the controlled release composition comprising xanthine derivatives and polyethylene oxide, as taught by Harrison, and produce the instant invention.

One of ordinary skill in the art would do this because there is no restriction on the drug used in the sustained release pharmaceutical preparation of Sako. One of ordinary skill in the art would apply the method of stabilizing a sustained or controlled release

pharmaceutical preparation with any active or drug. Since a controlled release pharmaceutical preparation comprising xanthine derivatives and polyethylene oxide was known in the art (as evidenced by Harrison), one of ordinary skill in the art would find it obvious to apply the method of stabilizing a controlled release pharmaceutical preparation for enhanced stability. Although Harrison does not expressly teach the elected species, it discloses the genus of xanthine derivatives in a controlled release preparation. One of ordinary skill in the art would find it obvious to incorporate the elected species, as disclosed by Hara, in a controlled release preparation with polyethylene oxide, because Harrison teaches that xanthine derivatives can be combined with polyethylene oxide.

Regarding instant claim 1, the xanthine compound represented by formula (IA) would have been obvious over the xanthine compound ((E)-8-(3,4-dimethoxystyryl)-1,3-diethyl-7-methylxanthine) taught by Hara (Page 3, [0027]). The method of suppressing dimerization would have been obvious over the stabilization of pharmaceutical compositions by adding iron oxide, as taught by Sako (Col. 2, lines 21-25) and over the controlled release device comprising drugs such as xanthine derivatives and polyethylene oxide as a suspending agent as taught by Harrison (Col. 5, lines 16-53, Col. 11, lines 8-31 and Col. 12, lines 55-66 and Examples 1, 2, 4 and 8).

Regarding instant claims 6-7, the elected species of the xanthine compound (E)-8-(3,4-dimethoxystyryl)-1,3-diethyl-7-methyl-3,7-dihydro-1H-purine-2,6-dione would have been obvious over the ((E)-8-(3,4-dimethoxystyryl)-1,3-diethyl-7-methylxanthine) taught by Hara (Page 3, [0027]).

Regarding instant claim 8, the limitation of the solid formulation with a core containing the xanthine compound and a coated layer containing the iron oxide would have been obvious over the tablets taught by Hara (Page 6, [0085]), in view of the yellow ferric oxide or red ferric oxide coated on a tablet, as taught by Sako (Col. 2, lines 21-25).

Regarding instant claims 10 and 12, the limitations of the percent by weight of iron oxide by weight of the coated layer would have been obvious over the 0.3 to 2 wt% of yellow ferric oxide and/or red ferric oxide in the film coating of the tablet taught by Sako (Col. 10, lines 52-53).

13. Claims 9 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hara et al. (WO 01/32182) in view of Sako et al. (US 6,562,375), Harrison et al. (US 5,573,776) and Okuda et al. (US 4,654,206).

Regarding the Hara reference, the corresponding US patent application publication (US 2005/0176739 A1 is being used as a reference since an English translation of the WIPO document (WO 01/32182) was not available.

The teachings of Hara, Sako, Harrison and Okuda are stated above.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make the xanthine compound ((E)-8-(3,4-dimethoxystyryl)-1,3-diethyl-7-methylxanthine), as taught by Hara, combine it with the method of stabilization of sustained release pharmaceutical preparations containing drugs and polyethylene

oxide by incorporating iron oxide, as taught by Sako, based on the controlled release composition comprising xanthine derivatives and polyethylene oxide, as taught by Harrison, further combine it with the use of iron oxide and inorganic substances in the coating layer of a solid pharmaceutical preparation, as taught by Okuda, and produce the instant invention.

One of ordinary skill in the art would do this because it would be obvious to try to include inorganic substances (disclosed by Sako) in the coating layer (taught by Okuda), and have a reasonable expectation of stabilizing the preparation containing the xanthine compound ((E)-8-(3,4-dimethoxystyryl)-1,3-diethyl-7-methylxanthine).

Regarding instant claim 9, the limitation of an inorganic substance in the coated layer would have been obvious over the additives that can be added to the iron oxide coated pharmaceutical compositions including talc, zinc oxide and magnesium oxide, as taught by Sako (Col. 6, line 58 to Col. 7, line 11) in view of the incorporation of talc and titanium oxide in the coating layer of solid preparations, as taught by Okuda (Col. 4, lines 36-40).

Regarding instant claim 11, the limitation of the coated layer containing 0.01 to 90 parts by weight inorganic substance per 100 parts by weight of the coated layer would have been obvious to one of ordinary skill in the art because during the process of routine experimentation, one would add different levels of the inorganic substances (such as talc, zinc oxide and magnesium oxide) that are taught by Sako (Col. 6, line 67 and Col. 7, lines 10-11) in view of the incorporation of talc and titanium oxide in the coating layer of solid preparations, as taught by Okuda (Col. 4, lines 36-40).

Conclusion

14. Due to the new grounds of rejection, this action is made non-final.

15. No claims are allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aradhana Sasan whose telephone number is (571) 272-9022. The examiner can normally be reached Monday to Thursday from 6:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached at 571-272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Aradhana Sasan/
Examiner, Art Unit 1615

/MP WOODWARD/
Supervisory Patent Examiner, Art Unit 1615